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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/763,276	01/26/2004	Masabumi Shibuya	BJS-249-323	6571
23117 7590 06/12/2007 NIXON & VANDERHYE, PC 901 NORTH GLEBE ROAD, 11TH FLOOR ARLINGTON, VA 22203			EXAMINER REDDIG, PETER J	
			ART UNIT 1642	PAPER NUMBER
			MAIL DATE 06/12/2007	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<p align="center"><b>Office Action Summary</b></p>	<b>Application No.</b> 10/763,276	<b>Applicant(s)</b> SHIBUYA ET AL.	
	<b>Examiner</b> Peter J. Reddig	<b>Art Unit</b> 1642	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 30 April 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,2,10,43 and 44 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,2,10,43 and 44 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>30 April 2007</u> . | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 30, 2007 has been entered.
2. An action on the RCE follows.
3. Claims 1, 2, 10, 43, and 44 are currently pending and under consideration.

### ***Rejections Maintained***

4. Claims 1, 2, 10, 43, and 44 remain rejected under 35 USC 112, first paragraph for the reasons previously set forth in the Office Actions of December 30, 2005, pages 3-5 and August 28, 2006 pages 2-3.

Applicants argue that the Examiner asserts that the previously submitted evidence "require that the antibody be injected into the cell or transfected into the cell to achieve the observed effects. The techniques are not applicable for in vivo/therapeutic use in which the antibody must be able to contact antigen presented on the surface of the cell." See page 2 of the Office Action dated August 28, 2006.

Applicants argue that the previously-submitted evidence (Declaration of Dr. Shitara submitted May 30, 2006) demonstrates that the cell growth of endothelial cells is inhibited by mixing the anti-PY1175 antibody with Chariot and contacting it with vascular cells. Applicants argue that the Examiner will appreciate that Chariot is also known as PEP-1 peptide having 21

Art Unit: 1642

amino acid residues, and is known to be a carrier peptide which transports a full-length protein in vivo and in vitro. See Abstract of attached Won Sik Eum et al, Free Radical Biology & Medicine Vol 37, No. 10, pp. 1656-1669 (2004)). Applicants argue that the attached Eum et al further teach that a fused polypeptide of antioxidant enzyme Cu, Zn-superoxide dismutase (SOD) and PEP-1 peptide is transduced in vivo in the skin (Fig 6) and in the neuronal cells of an ischemia animal model (Fig 7). Applicants argue that the it will therefore be clear to one of ordinary skill in the art that cell growth of endothelial cells is inhibited in vivo by administering to an animal a mixture of anti-PY1175 antibody having an in vitro effect with the known PEP-1 peptide (Chariot).

Applicants arguments have been carefully considered, but have not been found persuasive because the specification neither contemplates nor suggests administering antibody in combination with chariot and therefore the declaration is not commensurate in scope with the claimed invention because the method used in the declaration is not the same as the method taught in the specification as originally filed. Further, Eum et al. use a PEP-1-SOD fusion protein to transduce SOD into skin and neuronal cells, not a mixture of PEP-1 and the protein to be transduced as performed in the Declaration of Dr. Shitara submitted May 30, 2006, thus Eum et al. do provide support for the method Dr. Shitara being used in vivo as the methods are not commensurate in scope. Further, it is noted that the priority date of the instant application is January 24, 2001, three years prior to the publication date of the Eum et al. reference. Given that the claims are not drawn to fusion proteins or carrier peptides, given that the evidence of Eum et al. is not commensurate in scope with the claims and published three years post filing, Applicant's arguments have not been found persuasive and the rejection is maintained.

***Priority***

5. Acknowledgment is made of Applicant's claim for foreign priority based on an application filed in Japan on October 3, 2000, No. 2000-303694 and receipt of the a certified copy of the Japanese patent application No.2003-351259 as required by 35 U.S.C. 119(b). Acknowledgment is made of Applicant's submission of an English language translation of US Provisional Application 60/263,512 and a statement that it is accurate in Application 09/969, 037.

It is noted that, Examiner has established a priority date for the instant application, 10/763,276, of January 24, 2001 because the priority of the instantly claimed invention is based on the Japanese patent application No. 2000-303694 and the provisional application 60/263,512 both of which are in Japanese and have not been translated. Thus, the Examiner cannot determine if support for the instant application can be found in these documents. If Applicant disagrees with any rejection set forth in this action based on examiner's establishment of a priority date, January 24, 2001, for the instantly claimed application serial number 10/763,276, Applicant is invited to submit translation of the priority documents and to point to, page and line where support can be found establishing an earlier priority date. If applicant chooses to file a translation, then the translation must be filed together with a statement that the translation of the certified copy is accurate, see MPEP 201.15.

***New Grounds of Rejection***

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

Art Unit: 1642

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

6. Claims 1 and 2 are rejected under 35 U.S.C. 102(a) as being anticipated by Kanno et al. (Oncogene, April 20, 2000, 19:2138-46, IDS, see Appendix 1 for date) as evidenced by Takahashi et al. (EMBO J. 2001 20:2768-78).

The claims are drawn to:

1. A method for inhibiting KDR/Flk-1 signal transduction in endothelial cells, which comprises contacting the cells with a monoclonal antibody or an antibody fragment thereof, wherein said antibody and antibody fragment thereof specifically recognize 1175-tyrosine phosphorylated KDR/Flk-1.
2. A method for inhibiting cell growth, which comprises contacting the cells with a monoclonal antibody or an antibody fragment thereof, wherein said antibody and antibody fragment thereof specifically recognize 1175-tyrosine phosphorylated KDR/Flk-1.

It is noted that the claims are not limited to a monoclonal antibody that specifically recognize the phosphorylated tyrosine 1175 of KDR/Flk-1, but encompass monoclonal antibodies that specifically recognize KDR/Flk-1 that is phosphorylated at tyrosine 1175.

Kanno et al. teach a method for inhibiting VEGF stimulated endothelial cell proliferation and VEGF signal transduction to FAK and ERK1/2 using a monoclonal antibody to KDR that inhibits VEGF stimulated endothelial cell proliferation, see Figured 3, 7 and 8. Kanno et al teach this monoclonal antibody to KDR recognizes tyrosine phosphorylated KDR that has been stimulated with VEGF, Figure 2.

Takahashi et al. teach that tyrosine 1175 is a major site of tyrosine phosphorylation in KDR after VEGF treatment, see abstract, para bridging p. 2769-2770, and Fig. 3.

The methods of the prior art comprises the same methods as claimed in the instant invention, that is, a method for inhibiting KDR/Flk-1 signal transduction or cell growth in endothelial cells, which comprises contacting the cells with a monoclonal antibody or an antibody fragment thereof, wherein said antibody and antibody fragment thereof specifically recognize 1175-tyrosine phosphorylated KDR/Flk-1, thus the claimed methods are anticipated because the methods will inherently be methods for inhibiting KDR/Flk-1 signal transduction or cell growth in endothelial cells, which comprises contacting the cells with a monoclonal antibody or an antibody fragment thereof, wherein said antibody and antibody fragment thereof specifically recognize 1175-tyrosine phosphorylated KDR/Flk-1. See Ex parte Novitski 26 USPQ 1389 (BPAI 1993). Although the Kanno et al. reference does not specifically state that KDR was phosphorylated at tyrosine 1175, the claimed method appears to be the same as the prior art method, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed method. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed methods different from that taught by the prior art and to establish patentable differences. See In re Best, 562 F2nd 1252, 195 USPQ 430 (CCPA 1977).

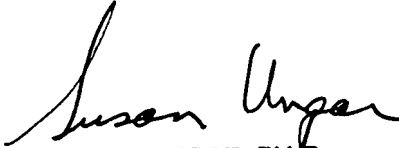
7. All other objections and rejections recited in the Office Action of August 28, 2006 are withdrawn.

Art Unit: 1642

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter J. Reddig whose telephone number is (571) 272-9031. The examiner can normally be reached on M-F 8:30 a.m.-5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on (571) 272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

  
SUSAN UNGAR, PH.D  
PRIMARY EXAMINER

Peter J. Reddig  
Examiner  
Art Unit 1642

PJR